

**EXHIBIT A:**

**MOUSE LKB1 COMPARED TO HUMAN LKB1**

## BLAST

## Basic Local Alignment Search Tool

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Blast 2 sequences

## SEQ ID NO: 6 (44-343) Compared to Mouse LKB1

Results for:

Your BLAST job specified more than one input sequence. This box lets you choose which input sequence to show BLAST results for.

## Query ID

[|c|41549](#)

[|c|41549](#)

## Description

SEQ ID NO: 6

## Molecule type

amino acid

## Query Length

433

## Subject ID

[|g|7106425\[ref\]\[NP\\_035622.1\]](#)

## Description

serine/threonine-protein kinase 11 [Mus musculus] >gi|81917862|sp|Q9WTK7.1|STK11\_MOUSE RefName: Full=Serine/threonine-protein kinase 11; AltName: Full=Serine/threonine-protein kinase LKB1 >gi|4838565|gb|AA031044.1|AF145287.1 Peutz-Jeghers syndrome kinase LKB1 [Mus musculus] >gi|649101|gb|AF21370.1|AF151711.1 protein kinase LKB1 [Mus musculus] >gi|4530575|gb|AA022100.1 serine/threonine-protein kinase LKB1 [Mus musculus] >gi|4589404|dbj|BAA76749.1|LKB1 [Mus musculus] >gi|5901683|gb|AA055368.1|Peutz-Jeghers syndrome protein [Mus musculus] >gi|30851173|gb|AAH52379.1|Serine/threonine kinase 11 [Mus musculus] >gi|74186437|dbj|BAE42977.1|unnamed protein product [Mus musculus] >gi|74192527|dbj|BAE43050.1|unnamed protein product [Mus musculus] >gi|117616790|gb|ABK42413.1|Stk11 [synthetic construct] >gi|14869953|gb|EDL31600.1|serine/threonine kinase 11, isoform CRA\_a [Mus musculus]

## Molecule type

amino acid

## Subject Length

436

## Program

BLASTP 2.2.24+ [Citation](#)

## Reference

Stephen F. Altschul, Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zheng, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", *Nucleic Acids Res.* 25:3389-3402.

## Reference - compositional score matrix adjustment

Stephen F. Altschul, John C. Wootton, E. Michael Gertz, Richa Agarwala, Aleksandr Morgulis, Alejandro A. Schäffer, and Yi-Kuo Yu (2005) "Protein database searches using compositionally adjusted substitution matrices", *FEBS J.* 272:5101-5109.

Other reports: [Search Summary](#) [Taxonomy reports](#) [Multiple alignment](#)

[Search Parameters](#)

## Search parameter name Search parameter value

Program	blastp
Query range	44-343
Word size	3
Expect value	10
Hitlist size	100
Gapcosts	11,1
Matrix	BLOSUM62
Low Complexity Filter	Yes
Filter string	L:
Genetic Code	1
Window Size	40
Threshold	11
Composition-based stats	2

Karlin-Altschul statistics

## Params Ungapped Gapped

Lambda	0.320459	0.267
K	0.136965	0.041
H	0.429592	0.14

## Results Statistics

## Results Statistics parameter name Results Statistics parameter value

Effective search space	110297
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## Graphic Summary

### Distribution of Blast Hits on the Query Sequence

[?]

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An overview of the database sequences aligned to the query sequence is shown. The score of each alignment is indicated by one of five different colors, which divides the range of scores into five groups. Multiple alignments on the same database sequence are connected by a striped line. Mousing over a hit sequence causes the definition and score to be shown in the window at the top, clicking on a hit sequence takes the user to the associated alignments. New: This graphic is an overview of database sequences aligned to the query sequence. Alignments are color-coded by score, within one of five score ranges. Multiple alignments on the same database sequence are connected by a dashed line. Mousing over an alignment shows the alignment definition and score in the box at the top. Clicking an alignment displays the alignment detail.

[Dot Matrix View](#)**Plot of |c|41549 vs g|7106425|ref|NP\_035622.1| [2]**

This dot matrix view shows regions of similarity based upon the BLAST results. The query sequence is represented on the X-axis and the numbers represent the bases/residues of the query. The subject is represented on the Y-axis and again the numbers represent the bases/residues of the subject. Alignments are shown in the plot as lines. Plus strand and protein matches are slanted from the bottom left to the upper right corner, minus strand matches are slanted from the upper left to the lower right. The number of lines shown in the plot is the same as the number of alignments found by BLAST.

**Descriptions**

Sequences producing significant alignments:	Score (Bits)	E Value
<a href="#">ref NP_035622.1 </a> serine/threonine-protein kinase 11 [Mus musc...	326	4e-154

**Alignments**

```
>ref|NP_035622.1| serine/threonine-protein kinase 11 [Mus musculus]
sp|Q9WFK1.1|STK11_MOUSE RefName: Full-Serine/threonine-protein kinase 11; AltName: Full-Serine/threonine-protein kinase LKB1
gb|AAD31044.1|AP145287.1 Peutz-Jeghers syndrome kinase LKB1 [Mus musculus]
9 more sequence titles

gb|AAP21370.1|AP151711.1 protein kinase LKB1 [Mus musculus]
gb|AAD21100.1| serine/threonine-protein Kinase LKB1 [Mus musculus]
db|BAAT6749.1| LKB1 [Mus musculus]
gb|AAD53568.1| Peutz-Jeghers syndrome protein [Mus musculus]
gb|AAH52379.1| serine/threonine kinase 11 [Mus musculus]
db|BAH42977.1| unnamed protein product [Mus musculus]
db|BAH43090.1| unnamed protein product [Mus musculus]
gb|BAK42413.1| stkl1 [synthetic construct]
gb|BDL31600.1| serine/threonine kinase 11, isoform CRA_a [Mus musculus]
length=436

Score = 526 bits (1354), Expect = 4e-154, Method: Compositional matrix adjust.
Identities = 288/300 (96%), Positives = 292/300 (98%), Gaps = 0/300 (0%)

Query 44 KLIGKYLMDLLGGSGYGVKEVLDSITLCRAVILKkkkllrIPNGEANVKKETQLLR 103
          KLIGKYLMDLLGGSGYGVKEVLDSITLCRAVILKkkkllrIPNGEANVKKETQLLR 103
Sbjct 44 KLIGKYLMDLLGGSGYGVKEVLDSITLCRAVILKkkkllrIPNGEANVKKETQLLR 103

Query 104 RLKHKRVIGLVLDVLYNEEKQKMYMVEYCVCGMQLDSVPEKRFPPVCGAHGYFQOLIDG 163
          RLKH+SVIGLVLDVLYNEEKQKMYMVEYCVCGMQLDSVPEKRFPPVCGAHGYF QOLIDG 163
Sbjct 104 RLKHKRVIGLVLDVLYNEEKQKMYMVEYCVCGMQLDSVPEKRFPPVCGAHGYFQOLIDG 163

Query 164 LEYLHSGQIVHKDIKPNllttgttLKISDLGVAAALHPFAADTCRTSQGSPAFCPPPE 223
          LEYLHSGQIVHKDIKPNllttgttLKISDLGVAAALHPFA DTCRTSQGSPAFCPPPE 223
Sbjct 164 LEYLHSGQIVHKDIKPNllttgttLKISDLGVAAALHPFAVDTCRTSQGSPAFCPPPE 223

Query 224 IANGLDTFSGFKVDIWSAGVTLYNITTGLYPPFGDNITKLFENIGKGSYAI PGDCGPPLS 283
          IANGLDTFSGFKVDIWSAGVTLYNITTGLYPPFGDNITKLFENIG+G + IP DCGPPLS 283
Sbjct 224 IANGLDTFSGFKVDIWSAGVTLYNITTGLYPPFGDNITKLFENIGKGGDTIPDCGPPLS 283

Query 284 DLLKMLLEYEPAKRFSTRQIRQNSWFRKKHHPA VPIPPSPUTKDRKNSMTVVPVLEED 343
          DLLKMLLEYEPAKRFSTRQIRQNSWFRKKHPLAALVPIPPSPUTKDRKNSMTVVPVLEED 343
Sbjct 284 DLLKMLLEYEPAKRFSTRQIRQNSWFRKKHPLAALVPIPPSPUTKDRKNSMTVVPVLEED 343
```

**EXHIBIT B:**

**MULTISPECIES COMPARISON OF STRAD POLYPEPTIDE**

## BLAST

## Basic Local Alignment Search Tool

[Edit and Resubmit](#) [Save Search Strategies](#) [Formatting options](#) [Download](#)

Blast 2 sequences

## STRAD comparison

Results for:

[ref|NP\_001003787.1| STE20-related kinase adapter protein alpha isoform 1 [Homo sapiens] >gi|74759034|sp|Q7RTN6.1|STRAA\_... (431aa) ▾]  
Your BLAST job specified more than one input sequence. This box lets you choose which input sequence to show BLAST results for.

## Query ID

gi|51242955|ref|NP\_001003787.1|  
gi|51242955|ref|NP\_001003787.1|

## Description

STE20-related kinase adapter protein alpha isoform 1 [Homo sapiens] >gi|74759034|sp|Q7RTN6.1|STRAA\_HUMAN RecName: Full=STE20-related kinase adapter protein alpha; Short=STRAD alpha; AltName: Full=STE20-related adapter protein; AltName: Full=Serologically defined breast cancer antigen NY-BR-96 >gi|34494889|sp|DAA01797.1| TPA\_exp: STE20-related adaptor protein [Homo sapiens] >gi|119614651|gb|EAW94285.1| protein kinase LYK5, isoform CRA\_c [Homo sapiens]

## Molecule type

amino acid

## Query Length

431

## Subject ID

4 subjects

## Description

## Molecule type

amino acid

## Subject Length

n/a

## Program

BLASTP 2.2.24+ [Citation](#)

## Reference

Stephen F. Altschul, Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997). "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", *Nucleic Acids Res.* 25:3389-3402.

[Reference - compositional score matrix adjustment](#)

Stephen F. Altschul, John C. Woitton, E. Michael Gertz, Richa Agarwala, Aleksandr Morgulis, Alejandro A. Schäffer, and Yi-Kuo Yu (2005). "Protein database searches using compositionally adjusted substitution matrices", *FEBS J.* 272:5101-5109.

Other reports: [Search Summary](#) [Taxonomy reports](#) [Distance tree of results](#) [Multiple alignment](#)

[Search Parameters](#)

## Search parameter name Search parameter value

Program	blastp
Word size	3
Expect value	10
Hittist size	100
Gspcoats	11,1
Matrix	BLOSUM62
Filter string	F
Genetic Code	1
Window Size	5
Threshold	11
Composition-based stats	2

Karlin-Altschul statistics

## Params Ungapped Gapped

Lambda	0.316819	0.267
K	0.13404	0.041
H	0.396234	0.14

Results Statistics

## Results Statistics parameter name Results Statistics parameter value

Effective search space	144800
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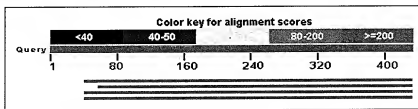
## Graphic Summary

### Distribution of 4 Blast Hits on the Query Sequence

[?]

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An overview of the database sequences aligned to the query sequence is shown. The score of each alignment is indicated by one of five different colors, which divides the range of scores into five groups. Multiple alignments on the same database sequence are connected by a striped line. Mousing over a hit sequence causes the definition and score to be shown in the window at the top, clicking on a hit sequence takes the user to the associated alignments. New: This graphic is an overview of database sequences aligned to the query sequence. Alignments are color-coded by score, within one of five score ranges. Multiple alignments on the same database sequence are connected by a dashed line. Mousing over an alignment shows the alignment definition and score in the box at the top. Clicking an alignment displays the alignment detail.



## Descriptions

Legend for links to other resources: [UniGene](#) [GEO](#) [Gene](#) [Structure](#) [Map Viewer](#) [PubChem BioAssay](#)  
Sequences producing significant alignments:

Accession	Description	Max score	Total score	Query coverage	E value	Links
<a href="#">XP_850260.1</a>	PREDICTED: similar to protein kinase LYK5 isoform 2 isoform 1 [Canis familiaris] STE20-related kinase adaptor protein alpha [Bos taurus] >g 124084523 ref NP_001155356.1 STE20-related kinase adaptor protein alpha [Ovis aries] >g 75070042 sp Q5E9J8.1 STRAA_BOVIN RecName: Full=STE20-related kinase adaptor protein alpha; Short=STRAD alpha; AltName: Full=STE20-related kinase adaptor protein >g 56565207 gb AAJ08938.1  protein kinase LYK5 isoform 4 [Bos taurus] >g 23856693 gb ACR46653.1  STRADA [Ovis aries] >g 296476245 gb DAA18360.1  STE20-related kinase adaptor protein alpha [Bos taurus] >ref NP_001155356.1  STE20-related kinase adaptor protein alpha [Ovis aries] >sp Q5E9J8.1 STRAA_BOVIN RecName: Full=STE20-related kinase adaptor protein alpha; Short=STRAD alpha; AltName: Full=STE20-related kinase adaptor protein >g AAJ08938.1  protein kinase LYK5 isoform 4 [Bos taurus] >g ACR46653.1  STRADA [Ovis aries] >g DAA18360.1  STE20-related kinase adaptor protein alpha [Bos taurus]	786	786	90%	0.0	<a href="#">UGM</a>
<a href="#">NP_001015603.1</a>	STE20-related kinase adaptor protein alpha [Mus musculus] >g 128475820 gb BA827626.1  unnamed protein product [Mus musculus] >g 33638094 gb AAQ24157.1  protein kinase LYK5 splice variant 1 [Mus musculus] >g 36182984 gb AAH59517.1  RIKEN cDNA 2610019A05 gene [Mus musculus] >g 117616948 gb ABK42491.1  STLKS [synthetic construct] >g 12343203 emb CAM27017.1  novel protein [Mus musculus] >g 148702325 gb EDL34272.1  RIKEN cDNA 2610019A05, isoform CRA_b [Mus musculus] >g 148702326 gb EDL34273.1  RIKEN cDNA 2610019A05, isoform CRA_b [Mus musculus] >g BA827626.1  unnamed protein product [Mus musculus] >g AAQ24157.1  protein kinase LYK5 splice variant 1 [Mus musculus] >g AAH59517.1  RIKEN cDNA 2610019A05 gene [Mus musculus] >g ABK42491.1  STLKS [synthetic construct] >emb CAM27017.1  novel protein [Mus musculus] >g EDL34272.1  RIKEN cDNA 2610019A05, isoform CRA_b [Mus musculus] >g EDL34273.1  RIKEN cDNA 2610019A05, isoform CRA_b [Mus musculus]	748	748	86%	0.0	<a href="#">UGM</a>
<a href="#">NP_082402.1</a>	STE20-related kinase adaptor protein alpha [Rattus norvegicus] >g 81912054 sp Q7TNZ6.1 STRAA_RAT RecName: Full=STE20-related kinase adaptor protein alpha; Short=STRAD alpha; AltName: Full=STE20-related kinase adaptor protein >g 8308721 gb U01811.1  protein kinase LYK5 [Rattus norvegicus] >sp Q7TNZ6.1 STRAA_RAT RecName: Full=STE20-related kinase adaptor protein alpha; Short=STRAD alpha; AltName: Full=STE20-related kinase adaptor protein >g AAP92801.1  protein kinase LYK5 [Rattus norvegicus]	775	775	90%	0.0	<a href="#">UGM</a>
<a href="#">NP_877972.1</a>	STE20-related kinase adaptor protein alpha [Rattus norvegicus] >g 81912054 sp Q7TNZ6.1 STRAA_RAT RecName: Full=STE20-related kinase adaptor protein alpha; Short=STRAD alpha; AltName: Full=STE20-related kinase adaptor protein >g 8308721 gb U01811.1  protein kinase LYK5 [Rattus norvegicus] >sp Q7TNZ6.1 STRAA_RAT RecName: Full=STE20-related kinase adaptor protein alpha; Short=STRAD alpha; AltName: Full=STE20-related kinase adaptor protein >g AAP92801.1  protein kinase LYK5 [Rattus norvegicus]	758	758	90%	0.0	<a href="#">UGM</a>

## Alignments

Select All [Get selected sequences](#) [Distance tree of results](#) [Multiple alignment](#)

```
>ref|XP_850260.1| UGM PREDICTED: similar to protein kinase LYK5 isoform 2 isoform 1
[Canis familiaris]
Length: 394

GENE ID: 609377 STRADA | STE20-related kinase adaptor alpha
[Canis lupus familiaris]

Score = 786 bits (2030), Expect = 0.0, Method: Compositional matrix adjust.
Identities = 376/390 (96%), Positives = 381/390 (98%), Gaps = 0/390 (0%)

Query 42 TNDASSESIASFQKSEKMSFPLPGGQCYELLTVIGKGFEDLMTVNLARYKPTGEVTVVRR 101
TH+ASSESIASFQKSEKMSFPLPGGQCYELLTVIGKGFEDLMTVNLARYKPTGEVTVVRR
Sbjct 5 TNDASSESIASFQKSEKMSFPLPGGQCYELLTVIGKGFEDLMTVNLARYKPTGEVTVVRR 64

Query 102 INLEACSNEMVTFLLQGLHVSFKLP+HPNI+PYRATFIADNELWVVTSPMAYGSAKDILCT 161
INLEACSNEMVTFLLQGLHVSFKLP+HPNI+PYRATFIADNELWVVTSPMAYGSAKDILCT
Sbjct 65 INLEACSNEMVTFLLQGLHVSFKLP+HPNI+PYRATFIADNELWVVTSPMAYGSAKDILCT 124

Query 162 HFMDGNGNELAIYAILQGVLCALDYIHHMGYVHRSVKASHILISVDQKVLISGLRSLNSLMI 221
HFMDGNGNELAIYAILQGVLCALDYIHHMGYVHRSVKASHILIS DGKVLISGLRSLNSLMI
Sbjct 125 HFMDGNGNELAIYAILQGVLCALDYIHHMGYVHRSVKASHILISDGKVLISGLRSLNSLMI 184

Query 222 SHGQRQRVHDFPKYSVKVLPWLSPEVLQNLQGYDAKSDIYSVGTACELANGHVFPFKD 281
SHGQRQRVHDFPKYSVKVLPWLSPEVLQNLQGYDAKSDIYSVGTACELANGHVFPFKD
Sbjct 185 SHGQRQRVHDFPKYSVKVLPWLSPEVLQNLQGYDAKSDIYSVGTACELANGHVFPFKD 244

Query 282 MPATQWLEKINGTVPCLLDTSTIPAEELTMSRS ANSGLSDSL TSTPRSHGSDSPS 341
MPATQWLEKINGTVPCLLDTSTIPAEELTMSRS ANSGLSDSL TSTPRSHGSDSPS
Sbjct 245 MPATQWLEKINGTVPCLLDTSTIPAEELTMSRS ANSGLSDSL TSTPRSHGSDSPS 304

Query 342 HPYHRTFSHPHHFVEQCLQRNPDPARSPASTLLNHSPFKQIKRRASEALPELLRPVTPIT 401
HPYHRTFSHPHHFVEQCLQRNPDPARSPASTLLNHSPFKQIKRRASEALPELLRPVTPIT
Sbjct 305 HPYHRTFSHPHHFVEQCLQRNPDPARSPASTLLNHSPFKQIKRRASEALPELLRPVTPIT 364

Query 402 NFEQSQSDHSGIFGLVTNLEELVDWDF 431
NFEQSQSDHSGIFGLVTNLEELVDWDF
```

Sbjct 365 NFEQSQPQDHSQIFGLVNTNLEELVDDWEF 394

>ref|NP\_001015603.1| **UGM** STE20-related kinase adapter protein alpha [Bos taurus]  
 ref|NP\_001155356.1| **UG** STE20-related kinase adapter protein alpha [Ovis aries]  
 sp|O58939.1|STRAA\_BOVIN RecName: Full=STE20-related kinase adapter protein alpha; Short=STRAD  
 alpha; AltName: Full=STE20-related adapter protein  
 gb|AAK08938.1| **G** protein kinase LYK5 isoform 4 [Bos taurus]  
 gb|ACR46653.1| **G** STRADA [Ovis aries]  
 gb|DAA18360.1| **G** STE20-related kinase adapter protein alpha [Bos taurus]  
 Length=373

GENE ID: 515024 STRADA | STE20-related kinase adaptor alpha [Bos taurus]  
 (10 or fewer PubMed links)  
 Score = 748 bits (1932), Expect = 0.0, Method: Compositional matrix adjust.  
 Identities = 356/373 (96%), Positives = 362/373 (98%), Gaps = 0/373 (0%)

Query 59 MSSFLPEGQCYELLTVIGKGFEDLMTVNLARYKPTGEYTVVRRINLEACSNEMVTLQGE 118  
 MSSFLPEGQCYELLTVIGKGFEDLMTVNLARYKPTGEYTVVRRINLEACSNEMVTLQGE  
 Sbjct 1 MSSFLPEGQCYELLTVIGKGFEDLMTVNLARYKPTGEYTVVRRINLEACSNEMVTLQGE 60  
 Query 119 LHVSKLPHNPIVPRATFIADNELWVTSFMYGSAKDILCTHFMDSMELAIATYILQ 178  
 LHVSKLP-HNPI-PY ATFIADNELWVTSFMYGSAKDILCTHFMDSMELAIATYILQ  
 Sbjct 61 LHVSKLPHNPIVPRATFIADNELWVTSFMYGSAKDILCTHFMDSMELAIATYILQ 120  
 Query 179 VLKALDYIHHMGYVHRSVKASHILISVDQKVLISGLRSLMSISHOQRQVRVHDPFKYSV 238  
 LKALDYIHHMGYVHRSVKASH+LIS DQKVLISGLRSLMSISHOQRQVRVHDPFKYS+  
 Sbjct 121 ALKALDYIHHMGYVHRSVKASHVILISADQKVLISGLRSLMSISHOQRQVRVHDPFKYSI 180  
 Query 239 KVLFWLSPVILQNLQGYDAKSDIYSGVITACELANGVHPFKDMPATCMLEKINGTVFC 298  
 KVLFWLSPVILQNLQGYDAKSDIYSGVITACELANGVHPFKDMPATCMLEKINGTVFC  
 Sbjct 181 KVLFWLSPVILQNLQGYDAKSDIYSGVITACELANGVHPFKDMPATCMLEKINGTVFC 240  
 Query 299 LLDITSTIPAEELTMSPSRSVANSGLSDSLTTPRPSNGDSPSHVYKRTSPHHPHFVQ 358  
 LLDITSTIPAEELTMSPSRS+ANGL+SL STPR SNQDSPSHVYKRTSPHHPHFVQ  
 Sbjct 241 LLDITSTIPAEELTMSPSRSVANSGLSESLTPRPSNGDSPSHVYKRTSPHHPHFVQ 300  
 Query 359 CLQRNPDARPSASTLLNHSFFKQIKRASEALPELLRPVTTITNFEQSQDHSQIFGLV 418  
 CLQRNPD RPSASTLLNHSFFKQIKRASEALPELLRPVTTIT FEQ OSQDHSQIFGLV  
 Sbjct 301 CLQRNPDARPSASTLLNHSFFKQIKRASEALPELLRPVTTITFEGRSQDHSQIFGLV 360  
 Query 419 TNLEELVDDWEF 431  
 TNLEELVDDWEF  
 Sbjct 361 TNLEELVDDWEF 373

>ref|NP\_062402.1| **UGM** STE20-related kinase adapter protein alpha [Mus musculus]  
 dbj|BAB27626.1| **G** unnamed protein product [Mus musculus]  
 gb|AAQ24157.1| **G** protein kinase LYK5 splice variant 1 [Mus musculus]  
 gb|AAH58517.1| **G** RIKEN cDNA 2610019A05 gene [Mus musculus]  
 gb|ABK42491.1| **G** STLK5 [synthetic construct]  
 emb|CAM27017.1| **G** novel protein [Mus musculus]  
 gb|BDL34272.1| **G** RIKEN cDNA 2610019A05, isoform CRA\_b [Mus musculus]  
 gb|BDL34273.1| **G** RIKEN cDNA 2610019A05, isoform CRA\_b [Mus musculus]  
 Length=394

GENE ID: 72149 Strada | STE20-related kinase adaptor alpha [Mus musculus]  
 (Over 10 PubMed links)  
 Score = 775 bits (2001), Expect = 0.0, Method: Compositional matrix adjust.  
 Identities = 369/390 (95%), Positives = 380/390 (98%), Gaps = 0/390 (0%)

Query 42 TNDASSIESIASPSKQFVMSFLPEGQCYELLTVIGKGFEDLMTVNLARYKPTGEYTVVRR 101  
 N+ASSIESIASPSK E+MSSFLPEGQCYELL+IGKGFEDLMTVNLARYKPTGEYTVVRR  
 Sbjct 5 ANEASSIESIASPSKPMSSFLPEGQCYELLTIGKGFEDLMTVNLARYKPTGEYTVVRR 64  
 Query 102 INLEACSNEMVTLQGEHLVSKLPHNPIVPRATFIADNELWVTSFMYGSAKDILCT 161  
 INLEACSNEMVTLQGEHLVSKLP+HNPIVPRATFIADNELWVTSFMYGSAKDIL T  
 Sbjct 65 INLEACSNEMVTLQGEHLVSKLPHNPIVPRATFIADNELWVTSFMYGSAKDILCT 124  
 Query 162 HFMDSMELAIATYILQGVKALDYIHHMGYVHRSVKASHILISVDQKVLISGLRSLMSI 221  
 HFMDSMELAIATYILQGVKALDYIHHMGYVHRSVKASHILISVDQKVLISGLRSLMSI  
 Sbjct 125 HFMDSMELAIATYILQGVKALDYIHHMGYVHRSVKASHILISVDQKVLISGLRSLMSI 184  
 Query 222 SHQGRQVRVHDPFKYSIKVLFWLSPVILQNLQGYDAKSDIYSGVITACELANGVHPFKD 281  
 SHQGRQR VHDFPKYS+KVLFWLSPVILQNLQGYDAKSDIYSGVITACELANGVHPFKD  
 Sbjct 185 SHQGRQVRVHDPFKYSIKVLFWLSPVILQNLQGYDAKSDIYSGVITACELANGVHPFKD 244  
 Query 282 MFATCMLEKINGTVFCILLDITSTIPAEELTMSPSRSVANSGLSDSLTTPRPSNGDSPS 341  
 MFATCMLEKINGTVFCILLDITSTIPAEELTMSPSRS+ANGL+DSL +RPSNGDSPS  
 Sbjct 245 MFATCMLEKINGTVFCILLDITSTIPAEELTMSPSRSIANGSLDLSANGSLRPSNGDSPS 304  
 Query 342 HPYHRTSPHHPHFVQCLQRNPDARPSASTLLNHSFFKQIKRASEALPELLRPVTTIT 401  
 HPYHRTSPHHPHFVQCLQRNPDARPSASTLLNHSFFKQIKRASEALPELLRPVTTIT  
 Sbjct 305 HPYHRTSPHHPHFVQCLQRNPDARPSASTLLNHSFFKQIKRASEALPELLRPVTTIT 364  
 Query 402 NFEQSQDHSQIFGLVNTNLEELVDDWEF 431  
 NFEQSQDHSQIFGLVNTNLEELVDDWEF  
 Sbjct 365 NFEQSQDHSQIFGLVNTNLEELVDDWEF 394

```

>ref|NP_877972.1| UGM STE20-related kinase adapter protein alpha [Rattus norvegicus]
sp|Q7TM26.1|STRAA_RAT G RecName: Full=STE20-related kinase adapter protein alpha; Short=STRAD
alpha; AltName: Full=STE20-related adapter protein
gb|AA092801.1| G protein kinase LYK5 [Rattus norvegicus]
Length=393

GENE ID: 303605 Strada | STE20-related kinase adaptor alpha [Rattus norvegicus]
(10 or fewer PubMed links)

Score = 758 bits (1958), Expect = 0.0, Method: Compositional matrix adjust.
Identities = 362/390 (93%), Positives = 377/390 (97%), Gaps = 1/390 (0%)

Query 42 TNDASSESTASFSKQEVMSFLPRGOCVELLTIVIGKGFEDLMTVNLARYKPTGRVYTVRR 101
Sbjct 5 N-ASSESTASFSY E-MSSFLPRGOCVELL-VIGKGFEDLMTVN -RYKPTGRVYTVRR 63

Query 102 INLEACSNEMVTFLGELHVS KLF+HPNTVPYRATFIADNELW VTSFMAVGS AKDLIT 161
Sbjct 64 INLEACSNEMVTFLGELHVS KLF+HPNTVPYRATFIADNELW VTSFMAVGS AKDLIT 123

Query 162 HFMDGMNELAJAIYILQGV LKALDYIHMGVYHRSVKASHILISVDGKVYLSGLRSLMSI 221
Sbjct 124 HFMDGMNELAJAIYILQGV LKALDYIHMGVYHRSVKASHILISVDGKVYLSGLRSLMSI 183

Query 222 SHGQGRVVRHDFPKYSKVLFWLSPEVLQNLQGYDAKSDIYSVGITACELANGHVFPFK 281
Sbjct 184 SHGQGRVVRHDFPKYSKVLFWLSPEVLQNLQGYDAKSDIYSVGITACELANGHVFPFK 243

Query 282 MPATQMLLEKLNKGTVPCLLDTSTIPAEELTMSPSRSVANSGLSDSLTTPSPNGSDSPS 341
Sbjct 244 MPATQMLLEKLNKGTVPCLLDTSTIPAEELTMSPSRSVANSGLSDSLTTPSPNGSDSPS 303

Query 342 HPYHRTFSPHFRHFVEQCLQRNPDPARPSASTLLNHSFFKQIKRRASEALPELLRPVTPIT 401
Sbjct 304 HPYHRTFSPHFRHFVEQCLQRNPDPARPSASTLLNHSFFKQIKRRASEALPELLRPVTPIT 363

Query 402 NFRSGSQDHSIGIFGLVTNLELEVDWDEF 431
Sbjct 364 NFRSGSQDHSIGIFGLVTNLELEVDWDEF 393

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**EXHIBIT C:**

**MULTISPECIES COMPARISON OF MO25 POLYPEPTIDE**



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All: 1 Fungi: 0 Mammals: 0

1: HomoloGene:69212. Gene conserved in Eukaryota

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## Pairwise Alignment Scores

Gene		Identity (%)		Substitution Rates <sup>1</sup>			
Species	Symbol	Protein	DNA	d	d <sub>N</sub> /d <sub>S</sub>	d <sub>NR</sub> /d <sub>NC</sub>	
<b>Homo sapiens</b>							
vs. Pan troglodytes	CAB39	100.0	99.9	0.001	0	0	Blast
vs. Canis lupus familiaris	CAB39	99.4	94.8	0.054	0	0	Blast
vs. Bos taurus	CAB39	100.0	94.0	0.062	0	0	Blast
vs. Mus musculus	Cab39	98.8	92.4	0.080	0	0	Blast
vs. Rattus norvegicus	Cab39	99.4	92.6	0.078	0	0	Blast
vs. Danio rerio	cab39	93.0	79.6	0.239	0	0	Blast
vs. Drosophila melanogaster	Mo25	71.9	63.8	0.494	0	0	Blast
vs. Anopheles gambiae	AgaP_AGAP000812	72.6	64.1	0.489	0	0	Blast
vs. Anopheles gambiae	AgaP_AGAP011060	73.3	64.8	0.476	0	0	Blast
vs. Caenorhabditis elegans	mop-25.1	65.3	61.7	0.537	0	0	Blast
vs. Caenorhabditis elegans	mop-25.2	61.2	60.5	0.561	0	0	Blast
vs. Schizosaccharomyces pombe	pmo25	51.7	55.7	0.669	0	0	Blast
vs. Arabidopsis thaliana	AT4G17270	44.7	52.4	0.756	0	0	Blast
vs. Arabidopsis thaliana	AT5G47540	43.5	52.5	0.753	0	0	Blast
vs. Oryza sativa	Os07g0585100	47.0	54.1	0.711	0	0	Blast
<b>Pan troglodytes</b>							
vs. Homo sapiens	CAB39	100.0	99.9	0.001	0	0	Blast
vs. Canis lupus familiaris	CAB39	99.4	94.8	0.054	0	0	Blast
vs. Bos taurus	CAB39	100.0	93.9	0.063	0	0	Blast
vs. Mus musculus	Cab39	98.8	92.3	0.081	0	0	Blast
vs. Rattus norvegicus	Cab39	99.4	92.5	0.079	0	0	Blast
vs. Danio rerio	cab39	93.0	79.6	0.239	0	0	Blast
vs. Drosophila melanogaster	Mo25	71.9	63.8	0.494	0	0	Blast
vs. Anopheles gambiae	AgaP_AGAP000812	72.6	64.1	0.489	0	0	Blast
vs. Anopheles gambiae	AgaP_AGAP011060	73.3	64.8	0.476	0	0	Blast
vs. Caenorhabditis elegans	mop-25.1	65.3	61.7	0.537	0	0	Blast
vs. Caenorhabditis elegans	mop-25.2	61.2	60.5	0.561	0	0	Blast
vs. Schizosaccharomyces pombe	pmo25	51.7	55.6	0.672	0	0	Blast
vs. Arabidopsis thaliana	AT4G17270	44.7	52.4	0.756	0	0	Blast
vs. Arabidopsis thaliana	AT5G47540	43.5	52.5	0.753	0	0	Blast
vs. Oryza sativa	Os07g0585100	47.0	54.1	0.711	0	0	Blast
<b>Canis lupus familiaris</b>							
vs. Homo sapiens	CAB39	99.4	94.8	0.054	0	0	Blast
vs. Pan troglodytes	CAB39	99.4	94.8	0.054	0	0	Blast
vs. Bos taurus	CAB39	99.4	93.5	0.067	0	0	Blast
vs. Mus musculus	Cab39	98.8	91.2	0.094	0	0	Blast

vs. <i>Rattus norvegicus</i>	Cab39	99.4	91.4	0.091	0	0	Blast
vs. <i>Danio rerio</i>	cab39	93.0	79.6	0.239	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	72.5	64.5	0.480	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	72.9	64.5	0.482	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	73.6	64.9	0.474	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	65.3	61.1	0.549	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	60.9	60.3	0.565	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	51.7	54.5	0.700	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	44.7	52.1	0.764	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	43.5	52.1	0.764	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	47.0	54.1	0.711	0	0	Blast
<b>Bos taurus</b>							
	CAB39						
vs. <i>Homo sapiens</i>	CAB39	100.0	94.0	0.062	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	100.0	93.9	0.063	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	99.4	93.5	0.067	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	98.8	91.6	0.089	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	99.4	92.0	0.085	0	0	Blast
vs. <i>Danio rerio</i>	cab39	93.0	79.4	0.241	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	71.9	65.7	0.458	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	72.6	65.4	0.465	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	73.3	66.2	0.450	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	65.3	61.7	0.537	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	61.2	60.6	0.559	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	51.7	53.8	0.718	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	44.7	52.1	0.764	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	43.5	52.5	0.753	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	47.0	54.5	0.701	0	0	Blast
<b>Mus musculus</b>							
	Cab39						
vs. <i>Homo sapiens</i>	CAB39	98.8	92.4	0.080	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	98.8	92.3	0.081	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	98.8	91.2	0.094	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	98.8	91.6	0.089	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	99.4	96.4	0.037	0	0	Blast
vs. <i>Danio rerio</i>	cab39	92.4	80.4	0.227	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	72.2	66.5	0.445	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	72.9	66.4	0.446	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	72.6	66.6	0.443	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	64.3	61.4	0.543	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	61.2	59.6	0.580	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	51.7	54.0	0.713	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	45.0	53.1	0.737	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	43.5	51.7	0.775	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	47.0	53.9	0.716	0	0	Blast
<b>Rattus norvegicus</b>							
	Cab39						
vs. <i>Homo sapiens</i>	CAB39	99.4	92.6	0.078	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	99.4	92.5	0.079	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	99.4	91.4	0.091	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	99.4	92.0	0.085	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	99.4	96.4	0.037	0	0	Blast
vs. <i>Danio rerio</i>	cab39	93.0	80.0	0.233	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	72.2	65.7	0.458	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	72.9	66.0	0.454	0	0	Blast

vs. <i>Anopheles gambiae</i>	AgarP_AGAP011060	72.6	65.9	0.455	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	64.3	61.2	0.547	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	61.2	59.8	0.576	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	51.7	53.7	0.720	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	44.7	52.2	0.761	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	43.5	51.5	0.781	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	47.0	54.2	0.708	0	0	Blast
<b>Danio rerio</b>	<b>cab39</b>						
vs. <i>Homo sapiens</i>	CAB39	93.0	79.6	0.239	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	93.0	79.6	0.239	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	93.0	79.6	0.239	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	93.0	79.4	0.241	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	92.4	80.4	0.227	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	93.0	80.0	0.233	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	69.5	68.8	0.404	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgarP_AGAP000812	70.9	69.4	0.393	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgarP_AGAP011060	70.6	67.8	0.421	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	63.8	62.1	0.529	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	60.9	61.1	0.548	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	51.7	52.5	0.753	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	45.3	53.2	0.734	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	43.8	52.1	0.764	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	47.0	53.7	0.722	0	0	Blast
<b>Drosophila melanogaster</b>	<b>Mo25</b>						
vs. <i>Homo sapiens</i>	CAB39	71.9	63.8	0.494	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	71.9	63.8	0.494	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	72.5	64.5	0.480	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	71.9	65.7	0.458	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	72.2	66.5	0.445	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	72.2	65.7	0.458	0	0	Blast
vs. <i>Danio rerio</i>	cab39	69.5	68.8	0.404	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgarP_AGAP000812	88.7	82.2	0.203	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgarP_AGAP011060	86.4	82.5	0.199	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	65.8	64.3	0.485	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	63.5	59.8	0.576	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	52.1	51.1	0.791	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	42.4	51.3	0.785	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	42.1	50.2	0.818	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	46.2	52.3	0.758	0	0	Blast
<b>Anopheles gambiae</b>	<b>AgarP_AGAP000812</b>						
vs. <i>Homo sapiens</i>	CAB39	72.6	64.1	0.489	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	72.6	64.1	0.489	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	72.9	64.5	0.482	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	72.6	65.4	0.465	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	72.9	66.4	0.446	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	72.9	66.0	0.454	0	0	Blast
vs. <i>Danio rerio</i>	cab39	70.9	69.4	0.393	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	88.7	82.2	0.203	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgarP_AGAP011060	93.7	90.7	0.100	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	66.2	64.9	0.474	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	62.0	61.8	0.534	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	50.9	50.1	0.821	0	0	Blast

vs. <i>Arabidopsis thaliana</i>	AT4G17270	43.1	51.1	0.793	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	43.3	49.8	0.830	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	46.0	51.6	0.776	0	0	Blast
<b>Anopheles gambiae</b>	<b>AgaP_AGAP011060</b>						
vs. <i>Homo sapiens</i>	CAB39	73.3	64.8	0.476	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	73.3	64.8	0.476	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	73.6	64.9	0.474	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	73.3	66.2	0.450	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	72.6	66.6	0.443	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	72.6	65.9	0.455	0	0	Blast
vs. <i>Danio rerio</i>	cab39	70.6	67.8	0.421	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	86.4	82.5	0.199	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	93.7	90.7	0.100	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	63.5	65.4	0.464	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	60.5	60.5	0.561	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	50.6	50.0	0.824	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	43.1	50.6	0.807	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	42.9	48.5	0.869	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	44.8	50.8	0.800	0	0	Blast
<b>Caenorhabditis elegans</b>	<b>mop-25.1</b>						
vs. <i>Homo sapiens</i>	CAB39	65.3	61.7	0.537	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	65.3	61.7	0.537	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	65.3	61.1	0.549	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	65.3	61.7	0.537	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	64.3	61.4	0.543	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	64.3	61.2	0.547	0	0	Blast
vs. <i>Danio rerio</i>	cab39	63.8	62.1	0.529	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	65.8	64.3	0.485	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	66.2	64.9	0.474	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	63.5	65.4	0.464	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	72.1	66.2	0.450	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	51.7	53.3	0.731	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	45.5	50.8	0.800	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	46.5	50.1	0.822	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	48.5	52.7	0.747	0	0	Blast
<b>Caenorhabditis elegans</b>	<b>mop-25.2</b>						
vs. <i>Homo sapiens</i>	CAB39	61.2	60.5	0.561	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	61.2	60.5	0.561	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	60.9	60.3	0.565	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	61.2	60.6	0.559	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	61.2	59.6	0.580	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	61.2	59.8	0.576	0	0	Blast
vs. <i>Danio rerio</i>	cab39	60.9	61.1	0.548	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	63.5	59.8	0.576	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	62.0	61.8	0.534	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	60.5	60.5	0.561	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	72.1	66.2	0.450	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	48.8	52.0	0.765	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	42.9	49.5	0.839	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	42.2	49.9	0.827	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	45.5	51.2	0.789	0	0	Blast
<b>Schizosaccharomyces pombe</b>	<b>pmo25</b>						

vs. <i>Homo sapiens</i>	CAB39	51.7	55.7	0.669	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	51.7	55.6	0.672	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	51.7	54.5	0.700	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	51.7	53.8	0.718	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	51.7	54.0	0.713	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	51.7	53.7	0.720	0	0	Blast
vs. <i>Danio rerio</i>	cab39	51.7	52.5	0.753	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	52.1	51.1	0.791	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	50.9	50.1	0.821	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	50.6	50.0	0.824	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	51.7	53.3	0.731	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	48.8	52.0	0.765	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	39.9	51.0	0.794	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	40.4	50.3	0.816	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	43.0	51.4	0.782	0	0	Blast
<b>Arabidopsis thaliana</b>		<b>AT4G17270</b>					
vs. <i>Homo sapiens</i>	CAB39	44.7	52.4	0.756	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	44.7	52.4	0.756	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	44.7	52.1	0.764	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	44.7	52.1	0.764	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	45.0	53.1	0.737	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	44.7	52.2	0.761	0	0	Blast
vs. <i>Danio rerio</i>	cab39	45.3	53.2	0.734	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	42.4	51.3	0.785	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	43.1	51.1	0.793	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	43.1	50.6	0.807	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	45.5	50.8	0.800	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	42.9	49.5	0.839	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	39.9	51.0	0.794	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	87.2	85.4	0.162	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	70.8	70.5	0.374	0	0	Blast
<b>Arabidopsis thaliana</b>		<b>AT5G47540</b>					
vs. <i>Homo sapiens</i>	CAB39	43.5	52.5	0.753	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	43.5	52.5	0.753	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	43.5	52.1	0.764	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	43.5	52.5	0.753	0	0	Blast
vs. <i>Mus musculus</i>	Cab39	43.5	51.7	0.775	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	43.5	51.5	0.781	0	0	Blast
vs. <i>Danio rerio</i>	cab39	43.8	52.1	0.764	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	42.1	50.2	0.818	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	43.3	49.8	0.830	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	42.9	48.5	0.869	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	46.5	50.1	0.822	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	42.2	49.9	0.827	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	40.4	50.3	0.816	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	87.2	85.4	0.162	0	0	Blast
vs. <i>Oryza sativa</i>	Os07g0585100	76.5	72.1	0.349	0	0	Blast
<b>Oryza sativa</b>		<b>Os07g0585100</b>					
vs. <i>Homo sapiens</i>	CAB39	47.0	54.1	0.711	0	0	Blast
vs. <i>Pan troglodytes</i>	CAB39	47.0	54.1	0.711	0	0	Blast
vs. <i>Canis lupus familiaris</i>	CAB39	47.0	54.1	0.711	0	0	Blast
vs. <i>Bos taurus</i>	CAB39	47.0	54.5	0.701	0	0	Blast

vs. <i>Mus musculus</i>	Cab39	47.0	53.9	0.716	0	0	Blast
vs. <i>Rattus norvegicus</i>	Cab39	47.0	54.2	0.708	0	0	Blast
vs. <i>Danio rerio</i>	cab39	47.0	53.7	0.722	0	0	Blast
vs. <i>Drosophila melanogaster</i>	Mo25	46.2	52.3	0.758	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP000812	46.0	51.6	0.776	0	0	Blast
vs. <i>Anopheles gambiae</i>	AgaP_AGAP011060	44.8	50.8	0.800	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.1	48.5	52.7	0.747	0	0	Blast
vs. <i>Caenorhabditis elegans</i>	mop-25.2	45.5	51.2	0.789	0	0	Blast
vs. <i>Schizosaccharomyces pombe</i>	pmo25	43.0	51.4	0.782	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT4G17270	70.8	70.5	0.374	0	0	Blast
vs. <i>Arabidopsis thaliana</i>	AT5G47540	76.5	72.1	0.349	0	0	Blast

<sup>1</sup> We present three rates for nucleotide substitutions per site, as defined below:

- $d$ : the number of nucleotide substitutions per site, corrected for multiple substitutions using the method of Jukes and Cantor (1969).
- $d_N/d_S$ : the ratio of the rate of nonsynonymous substitutions ( $d_N$ ) to the rate of synonymous substitutions ( $d_S$ ), calculated using the method of Nei and Gojobori (1986). A high value of this metric indicates adaptive selection, whereas a low value indicates purifying selection.
- $d_{NR}/d_{NC}$ : the ratio of radical nonsynonymous substitutions ( $d_{NR}$ ) to conservative nonsynonymous substitutions ( $d_{NC}$ ), calculated using the method of Hughes et al. (1990). This metric is analogous to  $d_N/d_S$ , but it has the advantage of being useful for studying the evolution of sequences that diverged in the distant past.

#### References

- Jukes TH, Cantor CR. Evolution of protein molecules. In: HN Munro, editor. Mammalian protein metabolism III. New York: Academic Press; 1969. p.21-132.
- Nei M, Gojobori T. Simple methods for estimating the numbers of synonymous and nonsynonymous nucleotide substitutions. Mol Biol Evol. 1986;3(6):418-26.
- Hughes AL, Ota T, Nei M. Positive Darwinian selection promotes charge profile diversity in the antigen-binding cleft of class I MHC molecules. Mol Biol Evol. 1990;7(6):515-24.

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**EXHIBIT D:**  
**COMPARISON OF RAT AND HUMAN LKB1**

**BLAST****Basic Local Alignment Search Tool**

•

[Edit and Resubmit](#) [Save Search Strategies](#) [Formatting options](#) [Download](#)

Blast 2 sequences

**SEQ ID NO: 6**Results for: 

Your BLAST job specified more than one input sequence. This box lets you choose which input sequence to show BLAST results for.

**Query ID**[|cd|17777](#)  
[|cd|17777](#)**Description**

SEQ ID NO: 6

**Molecule type**

amino acid

**Query Length**

433

**Subject ID**

gi|157820995|ref|NP\_001101539.1|

**Description**

serine/threonine-protein kinase 11 [Rattus norvegicus] &gt;gi|149034596|gb|EDL89333.1| serine/threonine kinase 11 (predicted), isoform CRA\_a [Rattus norvegicus]

**Molecule type**

amino acid

**Subject Length**

436

**Program**BLASTP 2.2.24+ [Citation](#)ReferenceStephen F. Altschul, Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", *Nucleic Acids Res.* 25:3389-3402.Reference - compositional score matrix adjustmentStephen F. Altschul, John C. Wootton, E. Michael Gertz, Richa Agarwala, Aleksandr Morgulis, Alejandro A. Schäffer, and Yi-Kuo Yu (2005) "Protein database searches using compositionally adjusted substitution matrices", *FEBS J.* 272:5101-5109.Other reports: [Search Summary](#) [Taxonomy reports](#) [Multiple alignment](#)[Search Parameters](#)**Search parameter name Search parameter value**

Program	blastp
Query range	44-343
Word size	3
Expect value	10
Hittlist size	100
Gapcosts	11,1
Matrix	BLOSUM62

Low Complexity Filter	Yes
Filter string	L;
Genetic Code	1
Window Size	40
Threshold	11
Composition-based stats	2

Karlin-Altschul statistics

**Params Ungapped Gapped**

Lambda	0.320459	0.267
K	0.139595	0.041
H	0.429592	0.14

Results Statistics

**Results Statistics parameter name Results Statistics parameter value**

Effective search space	110297
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**Graphic Summary****Distribution of Blast Hits on the Query Sequence**A placeholder box with a question mark icon and a horizontal line below it, indicating where a graphic summary would be displayed.

An overview of the database sequences aligned to the query sequence is shown. The score of each alignment is indicated by one of five different colors, which divides the range of scores into five groups. Multiple alignments on the same database sequence are connected by a striped line. Mousing over a hit sequence causes the definition and score to be shown in the window at the top, clicking on a hit sequence takes the user to the associated alignments. New: This graphic is an overview of database sequences aligned to the query sequence. Alignments are color-coded by score, within one of five score ranges. Multiple alignments on the same database sequence are connected by a dashed line. Mousing over an alignment shows the alignment definition and score in the box at the top. Clicking an alignment displays the alignment detail.

[Dot Matrix View](#)**Plot of lcl|17777 vs gi|157820995|ref|NP\_001101539.1| [?]**

This dot matrix view shows regions of similarity based upon the BLAST results. The query sequence is represented on the X-axis and the numbers represent the bases/residues of the query. The subject is represented on the Y-axis and again the numbers represent the bases/residues of the subject. Alignments are shown in the plot as lines. Plus strand and protein matches are slanted from the bottom left to the upper right corner, minus strand matches are slanted from the upper left to the lower right. The number of lines shown in the plot is the same as the number of alignments found by BLAST.

**Descriptions**

Sequences producing significant alignments:		Score (Bits)	E Value
<a href="#">ref NP_001101539.1 </a>	serine/threonine-protein kinase 11 [Rattus...	<a href="#">525</a>	1e-153

**Alignments**

>[ref|NP\\_001101539.1|](#) serine/threonine-protein kinase 11 [Rattus norvegicus]  
 gb|[EDL89333.1|](#) serine/threonine kinase 11 (predicted), isoform CRA\_a [Rattus norvegicus]  
 Length=436

Score = 525 bits (1351), Expect = 1e-153, Method: Compositional matrix adjust.  
 Identities = 287/300 (96%), Positives = 291/300 (97%), Gaps = 0/300 (0%)

Query	44	KLIGKYLMDGDLLEGSGYGVKEVLDSETLCRRRAVKILKKKLRRI	PNGEANVKKKEIQLLR	103
Sbjct	44	KLIGKYLMDGDLLEGSGYGVKEVLDSETLCRRRAVKILKKKLRRI	PNGEANVKKKEIQLLR	103
Query	104	RLRHKNVIQLVDVLYNNEEKQKMYMVMEYCVCGMQEMLDSVPEKRFPV	CQAHGYFCQLIDG	163
Sbjct	104	RLRHKNVIQLVDVLYNNEEKQKMYMVMEYCVCGMQEMLDSVPEKRFPV	CQAHGYFCQLIDG	163
Query	164	LEYLHSGQIVHKDIKPGnlllTtggtlKISDLGVAEALHPFAADDT	TCRTSQGSPAFOFPE	223
Sbjct	164	LEYLHSGQIVHKDIKPGnlllTtggtlKISDLGVAEALHPFAADDT	TCRTSQGSPAFOFPE	223
Query	224	IANGLDTFSGFKVDIWSAGVTLYNITTGLYPFEGDNIYKLFENIGKGSYA	IPGDCGPPLS	283
Sbjct	224	IANGLDTFSGFKVDIWSAGVTLYNITTGLYPFEGDNIYKLFENIG+G	+IPDCPFLS	283
Query	284	DLKGMLEYEPAKRFSIRQIRQHSWFRKKHppaeapvpippspDTKDRWRSMT	VVPYLED	343
Sbjct	284	DLKGMLEYEPAKRFSIRQIRQHSWFRKKHPLAEALVPIPPSPDTKDRWRSMT	VVPYLED	343